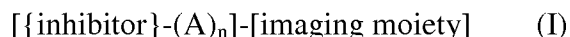


Listing of Claims:

1. (Currently amended) An *in vivo* imaging agent of Formula I:



where:

\{inhibitor\} is a synthetic barbituric acid matrix metalloproteinase inhibitor,
which is labeled at the 5-position of the barbituric acid with said
imaging moiety;

-(A)_n- is a linker group wherein each A is independently -CR₂-, -CR=CR-,
-C≡C-, -CR₂CO₂-, -CO₂CR₂-, -NRCO-, -CONR-, -NR(C=O)NR-,
-NR(C=S)NR-, -SO₂NR-, -NRSO₂-, -CR₂OCR₂-, -CR₂SCR₂-,
-CR₂NRCR₂-, a C₄₋₈ cycloheteroalkylene group, a C₄₋₈ cycloalkylene group, a
C₅₋₁₂ arylene group, or a C₃₋₁₂ heteroarylene group, an amino acid or a
monodisperse polyethyleneglycol (PEG) building block;

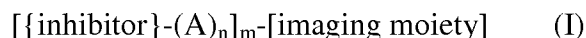
R is independently chosen from H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl,
C₁₋₄ alkoxyalkyl or C₁₋₄ hydroxyalkyl;

n is an integer of value 0 to 10;

wherein the imaging moiety can be detected externally in a non-invasive
manner following administration of said labelled synthetic barbituric acid
matrix metalloproteinase inhibitor to the mammalian body *in vivo*, and said
imaging moiety is chosen from:

- (i) a radioactive metal ion, which is a gamma emitter or a positron emitter
and is chosen from ^{99m}Tc, ¹¹¹In, ⁶⁴Cu, ⁶⁷Cu, ⁶⁷Ga or ⁶⁸Ga;
- ~~(ii) a paramagnetic metal ion;~~
- ~~(ii)(iii)~~ the a gamma-emitting radioactive halogen ¹²³I;
- ~~(iii)(iv)~~ a positron-emitting radioactive non-metal chosen from ¹⁸F, ¹¹C or ¹³N.
- ~~(v) hyperpolarised NMR active nucleus;~~
- ~~(vi) a reporter suitable for in vivo optical imaging.~~

2. (Cancelled) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor ligand conjugate is of Formula I:

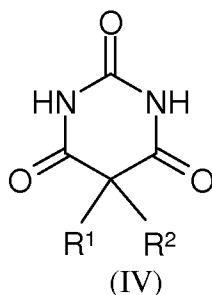


where:

{inhibitor} is the synthetic barbituric acid matrix metalloproteinase inhibitor;
 $-(A)_n-$ is a linker group wherein each A is independently $-\text{CR}_2-$, $-\text{CR}=\text{CR}-$, $-\text{C}\equiv\text{C}-$, $-\text{CR}_2\text{CO}_2-$, $-\text{CO}_2\text{CR}_2-$, $-\text{NRCO}-$, $-\text{CONR}-$, $-\text{NR}(\text{C}=\text{O})\text{NR}-$, $-\text{NR}(\text{C}=\text{S})\text{NR}-$, $-\text{SO}_2\text{NR}-$, $-\text{NRSO}_2-$, $-\text{CR}_2\text{OCR}_2-$, $-\text{CR}_2\text{SCR}_2-$, $-\text{CR}_2\text{NR}_2\text{CR}_2-$, a C_{4-8} cycloheteroalkylene group, a C_{4-8} cycloalkylene group, a C_{5-12} arylene group, or a C_{3-12} heteroarylene group, an amino acid or a monodisperse polyethyleneglycol (PEG) building block;
R is independently chosen from H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxyalkyl or C_{1-4} hydroxyalkyl;
n is an integer of value 0 to 10; and
m is 1, 2 or 3.

3. (Currently amended) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor is conjugated to a ligand, and said ligand forms a metal complex with the radioactive metal ion ~~or paramagnetic metal ion~~.
4. (Original) The imaging agent of Claim 3, where the ligand is a chelating agent.
5. (Cancelled) The imaging agent of Claim 3, where the radioactive metal ion is a gamma emitter or a positron emitter.
6. (Cancelled) The imaging agent of Claim 5, where the radioactive metal ion is $^{99\text{m}}\text{Tc}$, ^{111}In , ^{64}Cu , ^{67}Cu , ^{67}Ga or ^{68}Ga .
7. (Cancelled) The imaging agent of Claim 1, where the gamma-emitting radioactive halogen imaging moiety is ^{123}I .

8. (Cancelled) The imaging agent of Claim 1, where the positron-emitting radioactive non-metal is chosen from ^{18}F , ^{11}C or ^{13}N .
9. (Previously presented) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor is of Formula IV:



where:

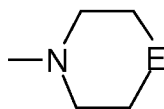
R^1 is R'' or a Z group;

R^2 is R'' , Y or $-\text{NR}^4\text{R}^5$, where R^4 is H or an R'' group, R^5 is H, C_{2-14} acyl, C_{2-10} aminoalkyl or (N- C_{2-14} acyl) C_{2-10} aminoalkyl or an R'' group, or R^4 and R^5 together with the N atom to which they are attached form an optionally (N- C_{2-14})acylated C_{2-8} cycloaminoalkylene ring;

R'' is independently C_{1-14} alkyl, C_{3-8} cycloalkyl, C_{2-14} alkenyl, C_{1-14} fluoroalkyl, C_{1-14} perfluoroalkyl, C_{6-14} aryl, C_{2-14} heteroaryl or C_{7-16} alkylaryl;

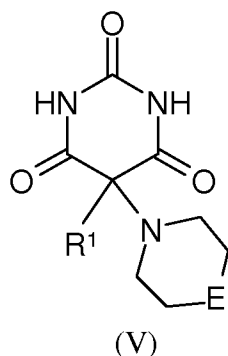
Z is a group of formula $-\text{A}^1\text{O}[\text{A}^2\text{O}]_p\text{R}^3$ where p is 0 or 1, and A^1 and A^2 are independently C_{1-10} alkylene, C_{3-8} cycloalkylene, C_{1-10} perfluoroalkylene, C_{6-10} arylene or C_{2-10} heteroarylene, and R^3 is an R group where R is independently chosen from H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxyalkyl or C_{1-4} hydroxyalkyl;

Y is a group of formula:



where E is CR_2 , O, S or NR^6 ; and R^6 is C_{2-14} acyl, or an R'' or Z group.

10. (Original) The imaging agent of claim 9, where R^2 is Y or $-NR^4R^5$.
11. (Previously presented) The imaging agent of claim 9, where the imaging moiety is attached to the R^2 substituent.
12. (Previously presented) The imaging agent of claim 9, of Formula V:

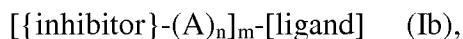


where E is CHR or NR^6 and R^1 is C_{6-14} *n*-alkyl, or C_{6-14} aryl.

13. (Original) The imaging agent of claim 12, where E is NR^6 and R^6 is C_{2-14} acyl; $-(CH_2)_dOH$, where d is 2, 3, 4 or 5; or $-C_6H_4X$, where X is H, C_{1-4} alkyl, Hal, OR, NR_2 , NO_2 or $SO_2NR^7R^8$, where R^7 and R^8 are independently R groups, and R is as defined in Claim 9.
14. (Previously presented) The imaging agent of claim 12, where R^1 is *n*-octyl, *n*-decyl, biphenyl, C_6H_5X or $-C_6H_4-O-C_6H_4X$ where X is as defined in Claim 13.
15. (Previously presented) A pharmaceutical composition which comprises the imaging agent of claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration.
16. (Currently amended) A radiopharmaceutical composition which comprises the imaging agent of claim 1 ~~wherein the imaging moiety is radioactive~~, together with a biocompatible carrier, in a form suitable for mammalian administration.

17. (Original) The radiopharmaceutical composition of claim 16, where the imaging moiety comprises a radioactive metal ion.
18. (Original) The radiopharmaceutical composition of claim 16, where the imaging moiety comprises a positron-emitting radioactive non-metal or a gamma-emitting radioactive halogen.
19. (Currently amended) A conjugate of a synthetic barbituric acid matrix metalloproteinase inhibitor with a ligand, wherein the barbituric acid comprises a 5-position substituent, and said 5-position substituent comprises a ligand capable of forming a metal complex with a radioactive ~~or paramagnetic~~ metal ion which is resistant to transchelation.
20. Original) The conjugate of Claim 19, of Formula Ib:
- $$[\{\text{inhibitor}\}-(A)_n]_m\text{-[ligand]} \quad (\text{Ib}),$$
- where {inhibitor}, A, n and m are as defined in Claim 2.
21. (Previously presented) The conjugate of Claim 19, wherein the synthetic barbituric acid matrix metalloproteinase inhibitor is of Formula IV or Formula V of Claims 9 to 14.
22. (Previously presented) The conjugate of Claim 19, wherein the ligand is a chelating agent.
23. (Original) The conjugate of Claim 22, wherein the chelating agent has a diaminedioxime, N_2S_2 , or N_3S donor set.
24. (Currently amended) A kit for the preparation of the radiopharmaceutical composition of Claim 17, which comprises a conjugate of a synthetic barbituric acid matrix metalloproteinase inhibitor with a ligand, wherein the barbituric acid comprises a 5-

position substituent, and said 5-position substituent comprises a ligand capable of forming a metal complex with a radioactive or paramagnetic metal ion which is resistant to transchelation, said conjugate being of Formula Ib:



where {inhibitor}, A, n and m are as defined in Claim 2, and wherein the ligand is a chelating agent.

25. (Original) The kit of Claim 26, where the radioactive metal ion is ^{99m}Tc , and the kit further comprises a biocompatible reductant.
26. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 18, which comprises a precursor in sterile form which is a non-radioactive derivative of the barbituric acid matrix metalloproteinase inhibitor of claims 1, wherein said non-radioactive derivative is capable of reaction with a source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen to give the desired radiopharmaceutical.
27. (Original) The kit of Claim 26, where the source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen is chosen from:
- (i) halide ion;
 - (ii) F^+ or I^+ ; or
 - (iii) an alkylating agent chosen from an alkyl or fluoroalkyl halide, tosylate, triflate or mesylate;
 - (iv) $\text{HS}(\text{CH}_2)_3^{18}\text{F}$.
28. (Previously presented) The kit of claim 26, wherein the non-radioactive derivative is chosen from:
- (i) an organometallic derivative such as a trialkylstannane or a trialkylsilane;

- (ii) a derivative containing an alkyl or aryl iodide or bromide, alkyl tosylate or alkyl mesylate for nucleophilic substitution;
- (iii) a derivative containing an aromatic ring activated towards nucleophilic or electrophilic substitution;
- (iv) a derivative containing a functional group which undergoes facile alkylation;
- (v) a derivative which undergoes alkylation with an alkyl thiol to give a thioether.

29. (Previously presented) The kit of claim 26, where the precursor is bound to a solid phase.

30. (Previously presented) Use of the imaging agent of Claim 1 for the diagnostic imaging of atherosclerosis.

31. (Previously presented) Use of the imaging agent of Claim 1 for the diagnostic imaging of unstable plaques.

32. (Previously presented) Use of the imaging agent of Claim 1 for the intravascular detection of atherosclerosis.